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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/095,536	06/10/1998	JOHN A. KINK	OPHD-03282	9749

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MEDLEN & CARROLL, LLP
101 HOWARD STREET
SUITE 350
SAN FRANCISCO, CA 94105

EXAMINER	
HISSONG, BRUCE D	
ART UNIT	PAPER NUMBER
1646	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/19/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	09/095,536	KINK, JOHN A.	
	Examiner	Art Unit	
	Bruce D. Hissong, Ph.D.	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 December 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *49-57* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *49-57* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Formal Matters

1. The Applicant's response to the office action mailed on 9/17/2006, including arguments/remarks and amended claims, was received on 12/21/2006 and has been entered into the record.

2. Claims 49-57 are currently pending and are the subject of this office action.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Rejection of claims 49-51 under 35 USC § 102(e) as being anticipated by Skurkovich *et al* (US 5,888,511), as set forth on pages 2-3 of the office action mailed on 9/17/2006, is *withdrawn* in response to Applicant's amendments to the claims to read on a method of treating a mammal having a plurality of symptoms of sepsis, wherein said symptoms comprise arterial hypotension. Skurkovich *et al* does not teach treatment of a mammal having a plurality of symptoms of sepsis, and does not specifically teach treatment of a mammal exhibiting arterial hypotension.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art

to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 49-57 are rejected under 35 U.S.C. 103(a) as being unpatentable over Skurkovich *et al* ("Skurkovich"), in view of Starnes *et al* ("Starnes" - *J. Immunol.*, 1990, Vol. 145, p. 4185-4191 – cited in the 7/2/99 office action), and further in view of Doherty *et al* ("Doherty" - *J. Immunol.*, 1992, Vol. 149, p. 1666-1670 – cited in the 7/2/99 office action).

The claims of the instant invention are drawn to a method of treating a mammal having a plurality of symptoms of sepsis, or a mammal having sepsis, or a mammal having septic shock, wherein said method comprises administering to said mammal a therapeutic composition comprising anti-TNF, anti-IL-6, and anti-IFN antibodies, and wherein said sepsis, symptoms of sepsis, or septic shock is reduced.

Skurkovich teaches a composition comprised of anti-TNF, anti-IL-6, and anti-IFN antibodies, but does not specifically teach administration of this composition for the treatment of a mammal having symptoms of sepsis, a mammal having sepsis, or a mammal having septic shock.

Starnes demonstrates a role for both IL-6 and TNF-α in mediating the pathogenesis of sepsis and septic shock (see abstract, p. 4185, 2nd column). Starnes also teaches that administration of neutralizing anti-TNF-α antibodies prevents mortality associated with septic shock (see Figure 4), and also inhibits IL-6 expression after E. coli exposure (p. 4185, last paragraph). Furthermore, Starnes discloses that administration of anti-IL-6 antibodies also protects against a lethal exposure to E. coli (see Figure 4).

Doherty demonstrates a role for both TNF-a and IFN-g in mediating the pathogenesis of sepsis and septic shock, and also teaches that administration of either anti-TNF-a or anti-IFN-g neutralizing antibodies protects against endotoxin lethality (see abstract, Figure 3).

Therefore, a person of ordinary skill in the art, at the time the instant invention was conceived, would have been motivated to administer the composition of Skurkovich to a mammal having symptoms of sepsis, having sepsis, or having septic shock. The motivation to do so comes from the fact that the combined teachings of Starnes and Doherty show that TNF-α, IL-6, and IFN-γ all play important roles in mediating the pathology of sepsis and septic shock, and that neutralization of each of these cytokines individually was shown to be effective in preventing LPS/endotoxin-mediated lethality (See MPEP 2144.06). Thus, one of ordinary skill in the art would have the motivation to administering a composition comprised of anti-IFN, anti-

IL-6, and anti-TNF antibodies (as disclosed in Skurkovich) to a mammal having symptoms of sepsis, having sepsis, or having septic shock.

> *In re Kerkhoven* (205 USPQ 1069, CCPA 1980) summarizes:
> "It is *prima facie* obvious to combine two compositions each of which is taught by prior art to be useful for the same purpose in order to form a combination that is to be used for the very same purpose: the idea of combining them flows logically from their having been individually taught in the prior art."

Furthermore, because the teachings of Starnes and Doherty demonstrate that IL-6, TNF-α, and IFN-γ all play important roles in mediating sepsis, one of ordinary skill in the art would have a reasonable expectation of success in reducing the symptoms of sepsis or septic shock by administering the composition taught by Skurkovich. In addition, although neither Starnes nor Doherty specifically recite reduction of symptoms such as arterial hypotension, metabolic acidosis, or organ failure, it is noted that Starnes does disclose these conditions as symptoms of gram-negative bacterium exposure/infection (see p. 4185, 1st paragraph), and that Starnes and Doherty both describe prevention of LPS-mediated lethality by inhibition of IL-6, TNF-a, and IFN-g. Thus, it would be expected, in the absence of evidence to the contrary, that a method of administering the composition of Skurkovich would inherently treat these symptoms in a mammal having sepsis or septic shock. Because the USPTO does not have the facilities for testing the composition of Skurkovich, the burden is on the Applicant to show a novel and unobvious difference between the claimed composition, and that of the prior art. See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray, 10 USPQ 2d 1922 1923 (PTO Bd. Pat. App. & Int.).

Conclusion

No claim is allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bruce D. Hissong, Ph.D., whose telephone number is (571) 272-3324. The examiner can normally be reached M-F from 8:30 am - 5:00 pm. If attempts to reach the

examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol, Ph.D., can be reached at (571) 272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

BDH
Art Unit 1646

ROBERT S. LANDSMAN, PH.D
PRIMARY EXAMINER